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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/562,191	10/26/2006	Vega Masignani	PP020667.0003	4113

27476 7590 06/24/2009

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EXAMINER	
FORD, VANESSA L	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
06/24/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/562,191	MASIGNANI ET AL.	
	Examiner	Art Unit	
	VANESSA L. FORD	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-23* is/are pending in the application.

4a) Of the above claim(s) *7-9,13-17 and 20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12/22/05* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/10/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is responsive to Applicant's election of Group I, claims 1-6, 10 and 18-19 and species SEQ ID No. 51 for examination in this application.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 7-9, 13-17 and 20-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 23, 2009. Claims 11-12 have been canceled.

Specification Objection

2. The use of the trademarks for example, Ribi™ and Detox™, page 10 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is asked to review the entire specification for these types of informalities and correction is required.

3. The specification is objected to for the following informalities: the specification recites "No^{s}" and should be changed to “Nos:”. See for example, page 2, line 14. Applicant is asked to review the specification for this types of informalities and correction is required.

4. The listing of references in the specification (pages 29-32) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

5. The drawings are objected to under 37 CFR 1.83(a) because they fail to show (indications of color changes) as described in the specification. See for example, page 16, Figure 30 of the instant specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure

is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

It should be remembered that color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 10 and 18-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions that are immunogenic compositions comprising the polypeptide as set forth in SEQ ID No.51 (elected sequence) does not reasonably provide enablement for pharmaceutical compositions that are vaccine compositions comprising the polypeptide as set forth in SEQ ID No.51. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Independent claim 1 is drawn to a polypeptide comprising one or more of: (a) an amino acid sequence selected from the group consisting of SEQ ID Nos. 51, 1, 2,3, 4, 5,6,7,8, 9, 10 ,11, 12, 13, 14, 15, 16 ,17, 18 and 54; (b) an amino acid sequence having at least 70% identity to a sequence as defined in (a); and/or (c) an amino acid sequence comprising a fragment of at least 8 consecutive amino acids of a sequence as defined in (a).

Independent claim 5 is drawn to a polypeptide of the formula NH2 A-$\{$-X-L$\}_x$-B-COOH.

Independent claim 6 is drawn to a polypeptide comprising the amino acid sequence -A-W_1-W_2-W_3-W_4-B.

Dependent claim 10 is drawn to a pharmaceutical composition comprising the polypeptide of claim 1.

Dependent claim 18 is drawn to a pharmaceutical composition comprising the polypeptide of claim 5.

Dependent claim 19 is drawn to a pharmaceutical composition comprising the polypeptide of claim 6.

The claimed invention encompasses pharmaceutical compositions, which are a broad group of compositions that include both immunogenic compositions as well as vaccine compositions. The instant specification teach that compositions of the invention are preferably immunogenic compositions and more preferably vaccine compositions (page 7). The specification teach that vaccines according to the invention may either be prophylactic (i.e. to prevent infection) or therapeutic (i.e. to treat infection) but will be typically prophylactic. (page 7).

The specification discloses adhesion and invasion experiments (pages 27-28). The specification has failed to show enablement for a pharmaceutical composition that is a vaccine composition. The specification fails to teach how to formulate and use pharmaceutical compositions that are vaccine compositions. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction.

The specification does not provide substantive evidence that the pharmaceutical compositions encompassed by the claims are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed

pharmaceutical compositions to treat or preventing *Haemophilus* infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the pharmaceutical compositions that are vaccine compositions , i.e. would not be able to accurately predict if protective immunity has been induced. Thus, the instant specification has not provided a pharmaceutical composition that is a vaccine composition.

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from in vitro antibody reactivity studies is problematic. Ellis (*Vaccines, W.B. Saunders Company, Chapter 29, 1988, pages 568-574)* exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of the at protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph). Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al *(Vaccines and Immunotherapy, 1991, Chapter 17),* wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response is induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine composition without the prior demonstration of vaccine efficacy. One of ordinary skill in the art would not reasonably conclude that the instant specification is enabled for a pharmaceutical composition that is a vaccine composition.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to developing a pharmaceutical compositions that are vaccine compositions that would achieve a desire level of success when administered to a patient with a *Haemophilus* that is capable of treating or preventing that *Haemophilus* infection, 3) there are no working examples which suggest that the claimed pharmaceutical compositions are vaccine compositions capable of treating or preventing *Haemophilus* infection, 4) the relative skill of those in the art is commonly recognized as quite high (post - doctoral level), and the lack of predictability in the field to which the invention pertains is recognized in the art as evidenced by the cited prior art.

In view of all of the above, in view of the lack of predictability in the art, it is determined that the instant specification is only enabled for a pharmaceutical composition that is an immunogenic composition and not a pharmaceutical composition

that is a vaccine composition. Therefore, Applicant has not met the requirements under 35 U.S.C. 112 first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1-6, 10 and 18-19 are rejected under 35 U.S.C. 102(a) anticipated by McGillivary et al *(103rd American Society for Microbiology General Meeting, Washington, D.C., USA, May 18-22, 2003, American Society for Microbiology)*.

Independent claim 1 is drawn to a polypeptide comprising one or more of: (a) an amino acid sequence selected from the group consisting of SEQ ID Nos. 51, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18 and 54; (b) an amino acid sequence having at least 70% identity to a sequence as defined in (a); and/or (c) an amino acid sequence comprising a fragment of at least 8 consecutive amino acids of a sequence as defined in (a).

Independent claim 5 is drawn to a polypeptide of the formula NH2 A-{-X-L}$_x$-B-COOH.

Independent claim 6 is drawn to a polypeptide comprising the amino acid sequence -A-W_1-W_2-W_3-W_4-B.

McGillivary et al teach a 86-kDa protein in strain F3031 of *Haemophilus aegyptius* (see the Abstract). McGillivary et al that strain F3031 causes Brazilian purpuric fever (BPF) (see the Abstract). McGillivary et al that the protein shares similar domains and at least some notable characteristics with proteins from several other organisms that are known to be important in virulence (see the Abstract). The amino acid sequence as et forth in SEQ ID NO.51 would be inherent in the teachings of the prior art. McGillivary et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptide). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

8. Claims 1-6, 10 and 18-19 are rejected under 35 U.S.C. 102(b) anticipated by Smoot et al *(Infection and Immunity, May 2002, Vo. 70, No. 2, pages 2694-2699).*

Independent claim 1 is drawn to a polypeptide comprising one or more of: (a) an amino acid sequence selected from the group consisting of SEQ ID Nos. 51, 1, 2,3, 4, 5,6,7,8, 9, 10 ,11, 12, 13, 14, 15, 16 ,17, 18 and 54; (b) an amino acid sequence having

at least 70% identity to a sequence as defined in (a); and/or (c) an amino acid sequence comprising a fragment of at least 8 consecutive amino acids of a sequence as defined in (a).

Independent claim 5 is drawn to a polypeptide of the formula NH2 A-{-X-L}$_x$-B-COOH.

Independent claim 6 is drawn to a polypeptide comprising the amino acid sequence -A-W_1-W_2-W_3-W_4-B.

Smoot et al teach DNA unique to *Haemophilus influenzae* Biogroup *aegyptius* strain F3031 which may encode novel virulence traits potentially involved in the pathogenesis of Brazilian purpuric fever (BPF) (page 2698). Smoot et al teach proteins that are homolog to *N. meningiditis* (page 2697, Table 3). It should be noted that the instant specification discloses that Smoot et al teach an incomplete NadA homolog which was found in BPF *Haemophilus influenzae* isolates. See page 20 of the instant specification. The instant specification teach that is polypeptide has been named HadA and the specification also discloses an alignment of the HadA protein with the NadA protein. See page 20 of the instant specification. Smoot et al anticipate the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's polypeptide with the polypeptide of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polypeptide of the prior art does not possess the same material structural and functional characteristics of the claimed polypeptide). See

In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Status of Claims

9. No claims allowed.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to VANESSA L. FORD whose telephone number is (571)272-0857. The examiner can normally be reached on 9 am- 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0756. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Vanessa L. Ford/
Examiner, Art Unit 1645
June 16, 2009